IMPACT OF SMOKING ON GLYCEMIC STATUS

DISSERTATION SUBMITTED FOR

M.D DEGREE (MEDICINE) BRANCH III

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CHENNAI

CERTIFICATE

This is to certify that the dissertation titled ***"IMPACT OF SMOKING ON GLYCEMIC STATUS"*** *submitted by* ***Dr. S. Ramu*** *to the Faculty of General Medicine, The Tamilnadu Dr. M.G.R. Medical university, Chennai in partial fulfillment of the requirement for the award of M.D. Degree Branch I (General Medicine) is a bonafide research work carried out by him under our direct supervision and guidance.*

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DECLARATION

I, **Dr. S. Ramu,** *solemnly declare that the dissertation titled* ***"IMPACT OF SMOKING ON GLYCEMIC STATUS"*** *has been prepared by me. I also declare, this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University, board either in India or abroad.*

This is submitted to the ***Tamilnadu Dr. M.G.R. Medical University****, Chennai in partial fulfillment of the rules and regulations for the M.D. Degree Examination in General Medicine to be held in March 2009.*

Place : Madurai

Date : **Dr.S.Ramu**

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CONTENTS

INTRODUCTION

Tobacco use has long been known to be a major risk factor for cardiovascular disease. Recent studies have identified a positive association between smoking and incidence of diabetes. The evidence that smoking is an independent risk factor for the development of diabetes is still considered preliminary. Some studies have shown a dose response association between smoking and incidence of diabetes; but others have not.

Several Hypothesis have been proposed to link tobacco use and incidence of diabetes. Smoking has been linked to impaired response to glucose tolerance tests and insulin resistance. Although, smoking cessation can result in modest weight gain, smoking is related to a more unhealthy distribution of upper body weight and greater waist – hip ratio. Smoking has also been associated with risk of chronic pancreatitis and pancreatic cancer, suggesting that tobacco smoke may be directly toxic to pancreas.

"Heavy smokers are more likely to get diabetes over time than are lighter smokers … who are in turn are more likely to get diabetes than non-smokers," said by Dr. William Ghali, one of the review authors.

While researchers are hesitant to directly link smoking to the onset of diabetes, they theorize that smoking may "lead to insulin resistance or inadequate compensatory insulin secretion responses," according to the authors, primarily from the University of Lausanne in Switzerland. Insulin resistance means. The body is less able to both store and process glucose, causing blood glucose levels to rise and leading to the development of Type 2 diabetes.

A number of preliminary studies have assessed the association between smoking and incidence of glucose abnormalities, suggesting that active smoking could be independently associated with glucose intolerance, impaired fasting glucose, and type 2 Diabetes.

REVIEW OF LITERATURE

CIGARETTE SMOKING

Cigarette smoking remains the most important cause of preventable morbidity and early mortality.

In 2000, there was an estimated 4.8 million premature deaths in the world attributable to smoking, 2.8 million in developing countries and 2 million in industrialised countries. More than 3/4 (3.8 million) of these deaths were in men. The leading causes of death from smoking were

Cardiovascular diseases	1.7 million deaths
COPD	1 million deaths
Lung cancer	0.9 million deaths(CMDT 2008)[2]

The incidence of smoking is highest in blacks, less educated persons and in the lower socio economic status. (Nicotine addiction – article by sat Sharma et al)[54]

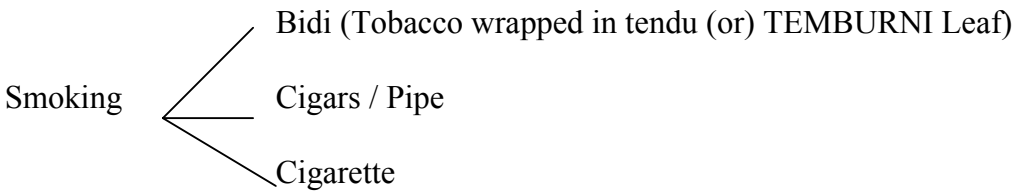
Tobacco addiction (p 2376-Harrison 17th edition)[1]

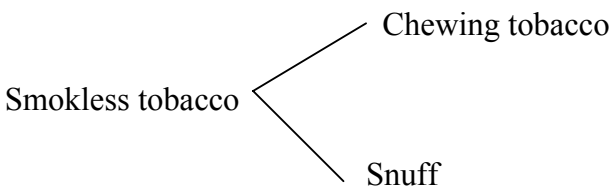
Nicotine, is the principle constituent of Tobacco responsible for its addictive character.

Addicted smokers regulate their Nicotine intake and blood levels by adjusting the frequency and intensify of their Tobacco use.

Nicotine is highly addictive, raises the Brain Level of Dopamine and alters the Bioavailability of Dopamine and Seratonin. It produces withdrawal symptoms on discontinuation.

FORMS OF TOBACCO USE





Smoking (Burned tobacco) – carcinogenic

Smokeless tobacco (unburned tobacco) – gum disease

Oral cancer

Slight increase in Heart disease

Bidi smoking is the most common form of tobacco smoking in India. The Bidi is an indigenous smoking stick 4-8cm long, usually containing 0.15 – 0.25g coarse tobacco flakes rolled in a rectangular piece of dried temburni

leaf. The number of bidis produced and consumed in India is 7-8 times higher than the number of cigarettes, thus most studies on health risks to smokers in India have concentrated on bidi smoking. Moreover, cigarette smoking is common generally only in higher socioeconomic groups. Besides cigarettes and bidis, other smoking habits includes various indigenous forms of pipe and cheroot smoking. Cheroots are small cigars made of heavy bodied cured tobacco rolled in a dried tobacco leaf and tied with a thread. (Shapiro et al)[55]

Chuttas are coarsely prepared cheroots. The length of chuttahs varies from 5 to 12 cm. The hookah. (Hooka) is a pipe that allows the tobacco smoke to pass through water before the smoker inhales it (Water pipe).

Cigarettes, cigars, spit and pipe tobacco are made from dried tobacco leaves, as well as ingredients added for flavor and other reasons. More than 4,000 different chemicals have been found in tobacco and tobacco smoke. Among them more than 60 chemicals known to cause cancer (carcinogens).

There are hundreds of substances added to cigarettes by manufacturers to enhance the flavor or to make smoking more pleasant. Some of the compounds found in tobacco smoke include ammonia, tar, and carbon monoxide. Exactly what effects these substances have on the cigarette

smoker's health is unknown, but there is no evidence that lowering the tar content of a cigarette lowers the health risk. Manufacturers do not usually give out information to the public about the additives used in cigarettes, so it is hard to know the health risks.

TYPE OF SMOKING AND ITS IMPACT

Pipes and Cigars

- Alkaline pH of smoke from blends of tobacco utilized for pipes and cigars allows significant absorption of Nicotine across oral mucosa.

- Therefore, they tend not to inhale the smoke into the Lung, confining the toxic and carcinogenic exposure largely to upper airway for most of these products.

Cigarettes and Bidis

Acidic pH of smoke from tobacco used in cigarettes and bidis induces Nicotine absorption in mouth.

Therefore, this favours inhalation of smoke in to larger surface of lungs in order to absorb quantities of Nicotine sufficient to satisfy smoker's addiction.

This leads to increased deposition in lungs

Increased Lung disease

Increased Lung cancer

Increased Heart disease

On comparing the above

- The risk of upper airway carcinoma is **similar among cigarette and cigar smokers**.

- While, those who have smoked only cigars, have a much lower risk of lung carcinoma, heart disease and COPD.

- However, cigarette smokers who switch to pipes / cigars do tend to inhale the smoke, increasing their risk.

Nicotine content (Jenifer et al 2001)[34]

Chewing tobacco (pan) 3.4 mg / g

Cigarettes

Filtered	16.3 mg /g
Unfiltered	13.5 mg / g
Bidis	21.2 mg / g

TYPE OF SMOKING AND ITS IMPACT

a)Bidis Vs Cigarettes

Since bidis contain a higher content of nicotine when compared to cigarettes, Smoking highlight **Bidi leads to more nicotine addiction**.

b)Filtered Vs unfiltered cigarettes

Smoking filtered cigarettes lowers disease risk. Smokers however can compensate and preserve their intake of nicotine by

- ❖ Changing the manner in which they smoke /puff on cigarette.
- ❖ The number of cigarettes smoked per day

Therefore, no meaningful disease – reduction benefit by smoking filtered cigarettes.

DISEASE MANIFESTATION IN SMOKING CIGARETTE

[P. 2736 – Harrison 17th edition [1], P.5 – CMDT 2008 [2]]

I. Cardiovascular disease (Large vessel atherosclerosis)

PVD (90%)

Aortic aneurysm (50%)

CAD (20 – 30%)

Occlusive cerebrovascular disease (10%)

Increased likelihood of MI and sudden cardiac death (since it promotes platelet aggregation and vascular occlusion)

II. Cancer

Ca. Lung

Ca.Oral cavity

Naso
Oro pharynx
Hypo

Nasal cavity

PNS

Larynx

Esophagus

Stomach

Pancreas

Ca.Kidney (Body + Pelvis)

Ureter

Urinary bladder

Uterine cervix

Liver

Acute myeloid leukemia

Increased risk for Colorectal cancer and Premenopausal Breast cancer

III. Respiratory Disease

COPD (90%)

IV. Pregnancy

Maternal complications

PROM

abruptio placentae

placenta praevia

spontaneous abortion

Fetal complications

Preterm delivery

Increased perinatal mortality

Small for gestational age

IRDS

Sudden infant death syndrome

V Other conditions

- Delayed healing of peptic ulcer
- Increase risk of osteoporosis

- ❖ Senile cataract
- ❖ Macular degeneration
- ❖ Premature menopause
- ❖ Skin wrinkling
- ❖ gall stones and cholecystitis
- ❖ Male impotence

VI. Environmental tobacco smoke

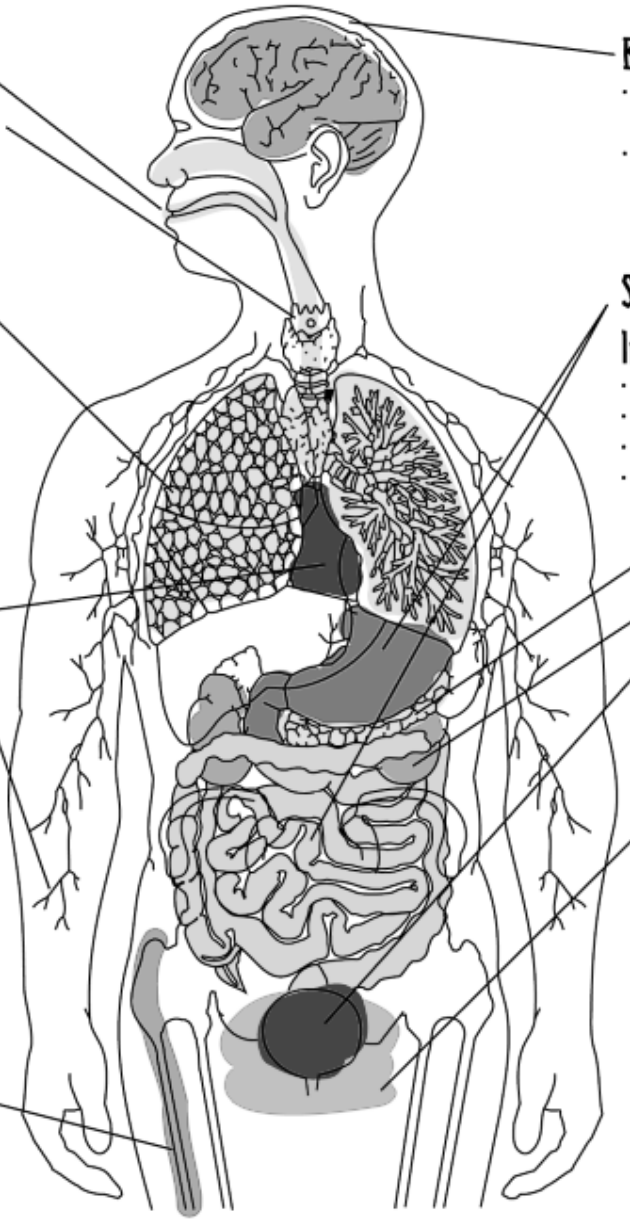
- ➢ Increased risk of lung carcinoma
- ➢ Increased risk of CAD
- ➢ Increased Resp tract infection
- ➢ CSOM
- ➢ Asthma exacerbation in children
- ➢ Increased cervical cancer
- ➢ Increased Invasive pneumococcal disease.

COMPARED TO NON SMOKERS

Smokers have

2 times risk for	fatal heart disease
10 times risk for	Lung carcinoma
Several times	Ca. Mouth / Throat / Esophagus / Pancreas / Kidney/ Bladder / Cervix
2 – 3 fold	Stroke / peptic ulcer
2 – 4 fold	Fracture Hip / wrist / Vertebrae
4 times	Invasive pneumococcal disease
2 fold	Cataract
2 – 5 times	ARMD (Age Related Macular degeneration)
increased risk of	Alzhemier's disease
Death	5 to 8 yrs earlier

The Long Term Health Effects Of Smoking Tobacco



Mouth, Lip, Throat, Larynx
- increased risk of cancer
- inflammation, laryngitis

Respiratory System
- bronchitis
- emphysema (chronic obstructive pulmonary disease)
- lung cancer

Circulatory System
- heart disease
- heart attack
- high blood pressure
- coronary artery disease (poor circulation in the legs causing ulcers, pain, and sometimes the need for amputation)

Bones
- brittle bones (osteoporosis)

Immune System
- depressed immune response
- increased infections

Brain
- increased risk of brain hemorrhage (stroke)
- women using contraceptive pill have an even greater risk of stroke

Stomach and Intestines
- lining becomes tender
- bleeding
- ulcers, slow to heal
- may lead to cancer

Pancreas, Kidney and Bladder
- increased risk of cancer

Reproductive System Male and Female
- decreased sperm count and movement
- lowered sex drive
- egg damage, irregular menstrual cycle and altered hormone levels
- cancers of the cervix, penis and anus
- early onset of menopause
- increased risk of breast cancer

Pregnancy and Babies
- lower than average birth weight
- high risk of Sudden Infant Death Syndrome
- increased risk of premature birth
- higher increased risk of miscarriage and still births
- increased risk of impairment in mental and physical development
- nicotine carried to baby in breast milk

DIABETES

(API text book of Medicine 8th edition – p. 1042) [3]

Diabetes Mellitus is a metabolic disorder characteristised by hyperglycemia resulting from defects in Insulin secretion, Insulin action on both. The prevalence of type & diabetes is increasing all over the world particularly in the developing countries. It has emerged as a major public health problem in our country. The WHO estimated that there were 31.7 million persons with diabetes in India in 2000 and that the number is likely to be 71.4 million in 2030. India has the distinction of having the largest number of diabetes in the world. Studies in 1980 highest prevalence rates of type & diabetes among migrant ethnic groups, suggesting that Indians as an ethnic group had a genetic propensity to develop diabetes which was precipitated by lifestyle changes. Current prevalence rates are 12.1% in the urban population. There is evidence that the prevalence of type 2 diabetes in increasing in rural population also.

Type 2 diabetes amongst Indians occurs at a younger age, the age at diagnosis being a decade earlier than in the west. Body mass indeed is lower by 4 kg/m2 in male and 6 kg/m2 in female. However abdominal obesity with increased waist to hip ratio is more common.

SMOKING AND DIABETES

There is a growing body of evidence that smoking is an Independent risk factor for diabetes, and that among people with diabetes, smoking aggravates the risk of serious disease and premature death.

In the Us Nurses Health Study, 114,247 women were followed for 8 years and 2,333 cases of type 2 diabetes were confirmed. After controlling for multiple risk factors, the relative risk of diabetes was 1.42 among women who smoked ≥ 25 cigarettes a day compared with non-smokers, suggesting a moderate association between smoking and the subsequent development of diabetes (Rimm, E.B. et al. 1993).[50]

A similar study of 41,810 middle aged men found that those who smoked > 25 cigarettes daily had a relative risk of diabetes of 1.94 compared with non smokers. (Rimm, E.B. et al 1995).[49]

A prospective study of Japanese men concluded that age of Smoking initiation and number of cigarettes smoked were major risk factors for developing diabetes (Kawakami, N. et al 1997).[35]

Similarly, data from the US cancer prevention study found that as smoking increased so the rate of diabetes increased for both men and women (Will JC et al. 2001).[70]

Another study found that smokers had a 44% increased risk of type 2 diabetes compared with non-smokers with the risk raising with number of cigarettes smoked.

The Journal of American Medical association study found the increased risk for those who smoked at least 20 cigarettes a day rose to 61%. For lighter smokers the risk was 29% higher than for a non smokers.

The findings from these studies are consistent with a positive association between the number of cigarettes smoked per day and the incidence of diabetes mellitus in both men and women. However, in the age-adjusted data, the evidence of a dose-response relation is limited and the effect is largely confined to those smoking more than two packs of cigarettes per day. The increased risk of diabetes observed in smokers remained significant on adjustment for potential confounders including body mass index (BMI) at baseline, alcohol use, race, amount of exercise, educational level and dietary intakes of fats and carbohydrate. On quitting smoking, rates of diabetes fell

gradually to that of non-smokers, providing some evidence of reversibility of the effect.

SMOKING AND HBA1C LEVELS

Given the problems of interpretation associated with prospective studies of incident cases of diagnosed diabetes, the data from Sargent et al. are illuminating. This work is based on cross-sectional analysis of the association between cigarette smoking and haemoglobin A_{1C} in 2704 men and 3358 women aged 45 to 74 who were recruited into the East Anglian component of the European Prospective Investigation into Cancer (EPIC-Norfolk). Participants with known diabetes were excluded from the analyses. Mean haemoglobin A_{1C} concentrations (a marker of long-term glucose homeostasis) were lowest in never smokers, intermediate in former smokers and highest in current smokers. There was a **'dose-response relationship between haemoglobin A_{1C} levels and both the number of cigarettes smoked per day and with total smoking as measured by pack-years'.** This association persisted in analysis adjusted for a range of potential confounders including BMI, waist-hip ratio, physical activity (based on an instrument with acceptable and well documented reliability and validity) and dietary variables, assessed using a standard food frequency questionnaire and plasma vitamin C concentration. In men, mean haemoglobin A_{1C} fell with increasing time since quitting smoking. The association between smoking and haemoglobin A_{1C}

levels persisted in analysis from which individuals reporting major illnesses were excluded.

Smoking and Insulin resistance

Smoking has also been identified as a risk factor for Insulin resistance which can lead to diabetes. Smoking may directly increase Insulin resistance. Insulin response to an oral glucose load was more pronounced in smokers than in non smokers. (Facchini Fs et al. 1992).[21] Insulin resistance was dose – dependently related to smoking (Eliasson B et al 1994).[19]

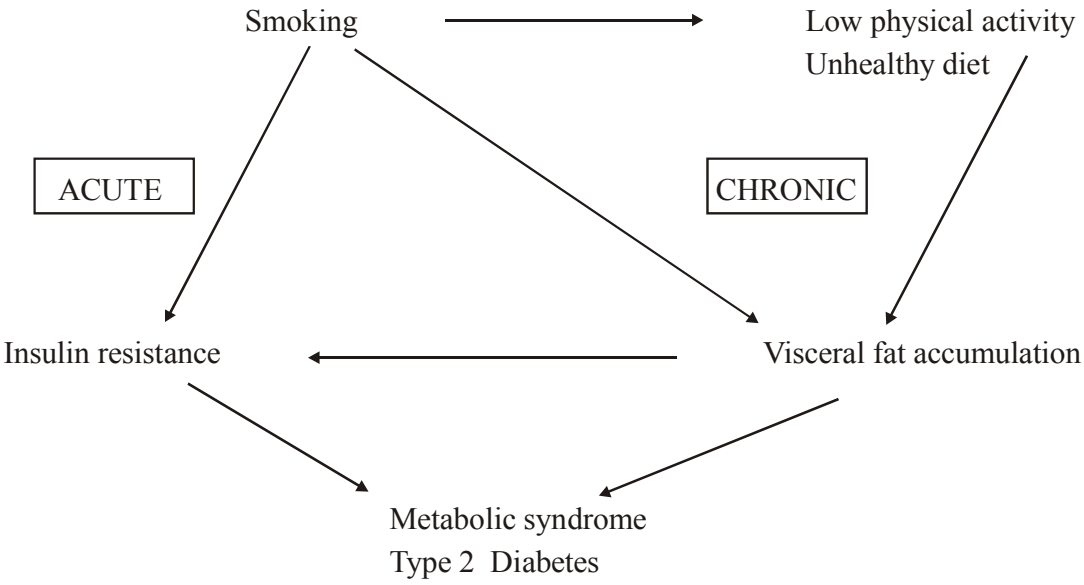
Further more smokers had features of Insulin resistance syndrome, including Low HDL cholesterol and high fasting glucose (Dzien et al 2004).[17]

Metabolic syndrome was shown to be associated with smoking. In a cross sectional study, male smokers had higher rates of metabolic syndrome than did non smokers (Geslain et al 2003).[24]

Among US adolescents 12 – 19 yrs old, the prevalence of metabolic syndrome increased with tobacco exposure. (Weitzman M et al 2005).[69]

Smoking leads to accumulation of visceral fat and then, to Insulin resistance. This association may be partly explained by a confounding with

low degree of physical activity and unhealthy diet frequently encountered among smokers.



Smoking and Waist Circumference

Waist circumference (WC) or Waist – Hip ratio (WHR) is an indicator of visceral adipose tissue (VAT). A greater amount of VAT is related to metabolic syndrome, diabetes and cardiovascular diseases (Han Ts et al 2006).[25] Cross-sectional studies indicate that WHR higher in smokers than in non-smokers. (Bamia C et al 2004).[7] WHR is positively associated with number of pack – years of smoking (Rosmond et al 1999)[51] and **'there is a dose response relation between WHR and the number of cigarettes smoked'.**

In particular, smokers had to have both a larger waist circumference and a smaller hip circumference than do non- smokers. This combination of high WHR and Low BMI is a "paradox" is found more frequent in smokers than in non-smokers.

The relationship between smoking and obesity is incompletely understood. On one hand, nicotine acutely increases energy expenditure (Hofstetter et al., NEJM 1986)[30] and could reduce apetite, which likely explains why smokers tend to have lower body weight than do nonsmokers and why smoking cessation is frequently followed by weight gain(Ward KD et al., 2001).[68]

Moreover, a popular belief among both smokers and nonsmokers is that smoking is an efficient way to control body weight(Potter BK et al., 2004).[45]On the other hand, studies indicate that heavy smokers(i.e., those smoking a greater number of cigarettes/day) have a greater body weight than do light smokers.

European congress of endocrinology 2006 evaluated the association between smoking and BMI, where they found that smokers had a lower BMI compared to nonsmokers. But among the smokers, BMI increased in proportion to the number of cigarettes smoked (cross sectional study). They have also done a longitudinal study, where they found that all smoking subgroups had an increased BMI.

At last they concluded by stating that, there is an U-shaped relationship between smoking and BMI. Heavy smoking is associated with an unhealthy lifestyle, which appeared to override the weight reducing effect of cigarette smoking.

Possible Mechanism

Smokers → Higher fasting plasma cortisol concentration that did non smokers (Cryer PE et al).[14]

↓

Influences Visceral adipose tissue.

The link between cigarette smoking and abnormalities of glucose Homeostasis is biologically plausible, as several studies have suggested that smoking may directly impair insulin sensitivity, One of the key determinants of glucose tolerance. (Ronnemaa T et al 1996).[52]

Smoking also found to reduce over all obesity but **accentuates central deposition of fat** (Slattery et al. 1993).[57] Another explanation for apparent effect of cigarette smoking on glucose tolerance would be through increased oxidative stress. This is known to be increased in cigarette smoking (Rahman I et al 1996)[48] and experimental evidence suggests that increased oxidative stress impair Insulin action. (Paolissa G et al 1996).[44]

In another large population – based study, **cigarette smoking was independently associated with higher HbA1C concentration in both men and women**. (Lincoln et al 2001).[38]

It has been found that smoking is a risk factor for type 2 diabetes, independently of BMI and physical activity [BMJ 2006; 332 (6 may)] [31]

The effect of smoking on the incidence of glucose intolerance occurred irrespective of waist hip ratio and baseline insulin that have been associated with development of diabetes. (Pederson et al).[45]

POSSIBLE MECHANISMS OF SMOKING & DIABETES

a)Smoking → activates sympathetic system → Higher fasting plasma

↓ Cortisol concentration

Increased catecholamines ↓

↓ influences visceral adipose tissue

Inhibits insulin mediated Uptake of glucose ↓

↓

Insulin resistance insulin resistance

b)Smoking → Low physical activity and unhealthy diet

↓

Visceral fat accumulation → insulin resistance

c)Smoking → direct influence on insulin sensitivity by increasing oxidative stress

↓

impaired insulin action

d) smoking → metabolic syndrome

SMOKING IN DIABETES

Smokers are insulin resistant, exhibit several aspects of the insulin resistance syndrome, and are at an increased risk for type 2 diabetes.

Many patients with type 1 and type 2 diabetes mellitus are at risk for micro- and macrovascular complications.

Cigarette smoking increases this risk for diabetic nephropathy, retinopathy, and neuropathy, probably via its metabolic effects in combination with increased Inflammation and endothelial dysfunction. This association is strongest in type 1 diabetic patients.

The increased risk for macrovascular complications, coronary heart disease (CHD), stroke, and peripheral vascular disease, is most pronounced in type 2 diabetic patients.

The development of type 2 diabetes is another possible consequence of cigarette smoking, besides the better-known increased risk for cardiovascular disease. In diabetes care, smoking cessation is of utmost importance to

facilitate glycemic control and limit the development of diabetic complications.

BENEFITS OF SMOKING CESSATION

There is an overwhelming evidence that stopping smoking reduces the risk of cardiovascular disease, lung disease, cancer and stroke (Us department of health and human services 1990).[63]

As diabetes increases the risk for heart disease and stroke, it follows that stopping smoking will reduce the risk of complications from diabetes such as heart disease.

Few studies have evaluated smoking cessation treatment specifically for people with diabetes but the limited research available suggests that smokers with diabetes may be less successful in quitting than smokers without diabetes and that intensive strategies should be considered to optimise successful cessation(Haire-josu D et al.,1999)[28]

One possible explanation for the lower quitting rates among people with diabetes is the fact that stopping smoking is associated with weight gain and this is likely to be of concern in people who have diabetes and are already overweight.

One US study found that concerns about weight gain among smokers with Type 1 diabetes were particularly prevalent among women, obese smokers, and those in poor metabolic control(Haire-joshu D et al)[27] Fear of weight gain was cited by 49% of smokers.

A recent British prospective study of 7,735 men aged 40-59 years found that cigarette smoking was associated with a significant increase in risk of diabetes, even after adjustment for age, body mass index, and other potential confounding factors. The benefit of giving up smoking was only apparent after 5 years of smoking cessation and risk reverted to that of never-smokers only after 20 years. Men who gave up smoking during the first 5 years of follow-up showed significant weight gain and subsequently higher risk of diabetes than continuing smokers. However, the authors concluded that in the long term, the benefits of giving up smoking outweigh the adverse effects of early weight gain(Wannamethee SG et al .,2001)[66]

Stopping smoking also reduces the risk of premature death. The US Nurses' Study found that among women with Type 2 diabetes who had stopped smoking for 10 or more years had a mortality relative risk of 1.11 compared with diabetic women who were never smokers (Al Delaimy W.K. et al 2001)[4]

In the light of the growing evidence demonstrating that smoking is an independent risk factor for diabetes and that it is also an aggravating factor for diabetes complications, smoking cessation advice should be a routine component of diabetic care. Concerns about weight gain should be addressed by health care providers whilst emphasising the fact that the health benefits of smoking cessation far outweigh post cessation weight gain, even in people who are focused on weight management.

AIM OF THE STUDY

AIM OF THE STUDY

- To assess whether smokers are more likely than non smokers to develop clinically relevant glucose intolerance or diabetes.
- To assess whether total pack years correlates with the severity of glucose intolerance/ diabetes.
- To assess whether the various types of tobacco smoking (Bidis, Cigarettes or both) have an influence on the development of glucose intolerance / diabetes.
- To assess the relationship between smoking and obesity and thereby to find an indirect evidence of insulin resistance.

MATERIALS AND METHODS

MATERIALS AND METHODS

Design of study	**:**	Cross sectional study
Period of study	**:**	June 2007 – June 2008
Sample size	**:**	150 patients
Selection of subjects	**:**	Patients attending Government Rajaji Hospital of age 18 – 60 yrs.
Data Collection	**:**	Socio demographic Clinical Biochemical Anthropometry
Methods	**:**	Standard clinical and laboratory methods.
Consent	**:**	Informed consent was obtained from all patients or relatives.

Inclusion Criteria

All smokers attending Govt. Rajaji Hospital from 18 – 60 years of age.

Exclusion criteria

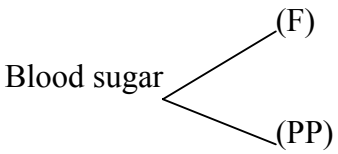
- ❖ Known diabetes
- ❖ Alcoholics
- ❖ Pregnancy
- ❖ Age < 18 and > 60 years.
- ❖ Acute stressful situations such as
    - Myocardial infarction
    - Trauma
    - Severe Infection
- ❖ Patients on drugs such as
    - Steroids
    - OCP
    - Thiazide diuretics

Clinical materials

- Weight
- Height
- BMI
- Waist circumference
- Hip circumference
- Waist hip ratio

Laboratory materials

The following investigations were done for all the patients



Fasting Lipid profile

TC

TGL

HDL

VLDL

LDL

Methods

We have evaluated HUNDRED smokers and FIFTY nonsmokers Baseline characteristics of the study are as follows; age, sex, occupation, Education status, family history of diabetes, comorbid illness of smoking. Our Baseline examination included Ht, Wt, BMI, BP, HC, WC, Waist Hip ratio (anthropometric measurements), Lab investigation – Blood sugar (F and PP) and Lipid profile

Definition of Baseline tobacco exposure

Participants were defined as current smokers and former smokers. Former smoker were those who, at baseline, reported previously using cigarettes but denied current smoking.

Definition of outcomes

Guidelines from the American Diabetes association defined

Impaired fasting glucose as serum glucose

≥100mg / dl and < 126 mg / dl

Diabetes as fasting serum glucose

≥ 126 mg / dl

Body mass index defined as $\frac{\textbf{Wt (kg)}}{\textbf{Ht (m}^2\textbf{)}}$

Normal < 25 kg / m^2

Over weight 25.0 – 29.9

Obesity ≥ 30

Extreme obesity ≥ 40

Pack Years is defined as

$$\frac{\text{Number of cigarettes smoked per day} \times \text{Numbers of years smoked}}{20}$$

Metabolic syndrome : NCEP : ATPIII 2001 guidelines

Presence of ≥ 3 of the following is diagnostic of metabolic syndrome

- Central obesity : Waist circumference > 102 cm (M) / > 88cm (F)
- Increased Triglycerides : Fasting Triglycerides > 150mg / dl
- Decreased HDL : < 40 mg / dl (Male)
  < 50 mg / dl (Female)
- Hypertension : Blood pressure Systolic BP≥ 130mmHg
  (or)
  Diastolic ≥ 85 mg
- Fasting plasma glucose : ≥ 100mg / dl (or) previously diagnosed type 2 DM

RESULTS

RESULTS

A. PROFILE OF CASES STUDIED

Table 1

Age Distribution

Age Groups	Smokers – 100		Non Smokers – 50	
	No	**%**	**No**	**%**
Upto 30 years	7	7	2	4
31 – 40 years	23	23	5	10
41 – 50 years	32	32	28	56
51 – 60 years	38	38	15	30
Total	100	100	50	100
Mean	47.34 Years		47.62 Years	
S.D	10.76 years		6.89 years	
'p' value	0.8091 Not significant			

Age of the study population ranged from 15 – 65 years. Majority of them were between 3rd and 5th decade (85%). Mean age of cases were 47.34 in our study. Mean age of controls were 47.62 in our study. Thus there was no significant difference between cases and controls with respect to age ('p' = 0.80)

AGE DISTRIBUTION

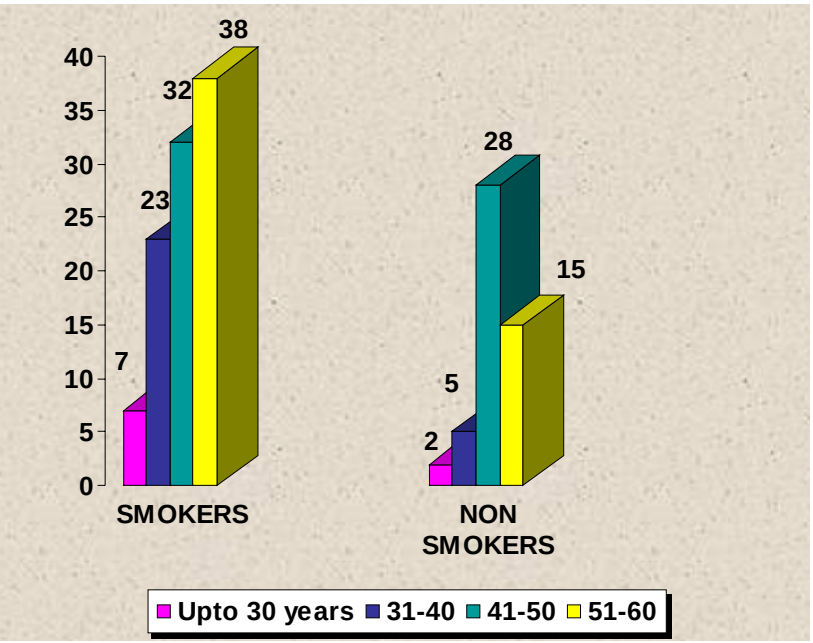


Table 2

Occupation

Occupation	Smokers = 100		Non Smokers = 50	
	No	%	No	%
Agriculture	14	14	5	10
Drivers	11	11	-	-
Carpenter	4	4	-	-
Daily wages labourer	43	43	33	66
Dhoby	5	5	1	2
Merchants	2	2	-	-
Load man	18	18	7	14
Engineer	1	1	-	-
Clerks	2	2	4	8

Majority of the case population were daily wages labourer (43%), followed by other workers (18%), which included barbers and mechanics. Among the control population, majority of them were daily wages labourer (66%).

Table 3

Educational Status

Occupation	Cases (Smokers)		Controls (Non Smokers)	
	No	**%**	**No**	**%**
Illiterates	2	21	8	16
Upto 5th std	45	45	21	42
6 – 8 th std	19	19	14	28
9 – 12th std	14	14	7	14
B.E	1	1	-	-
Total	100	100	50	100

Majority of the case population were found to be educated upto 5th standard (45%). Nearly 21% of the case population were found to be illiterate.

EDUCATIONAL STATUS

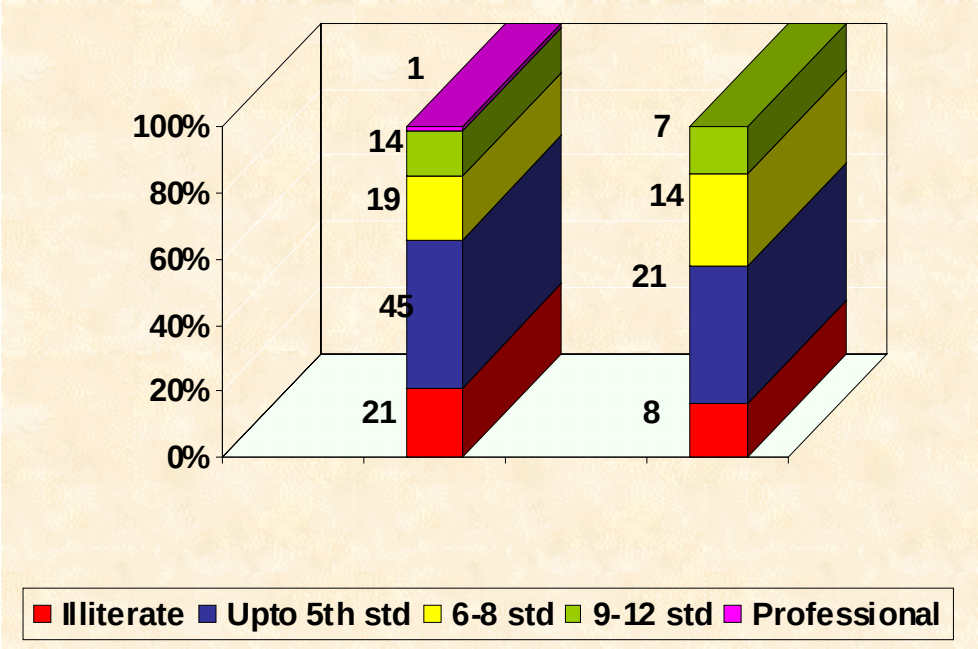


Table 4

Family History of Diabetes

Family History	Cases (Smokers)		Controls (Non Smokers)	
	No	**%**	**No**	**%**
Yes	4	4	-	-
No	96	96	50	100
P	0.3016 Not Significant			

Among the study population, only 4% of the cases were found to have family history of diabetes.

FAMILY HISTORY OF DIABETES

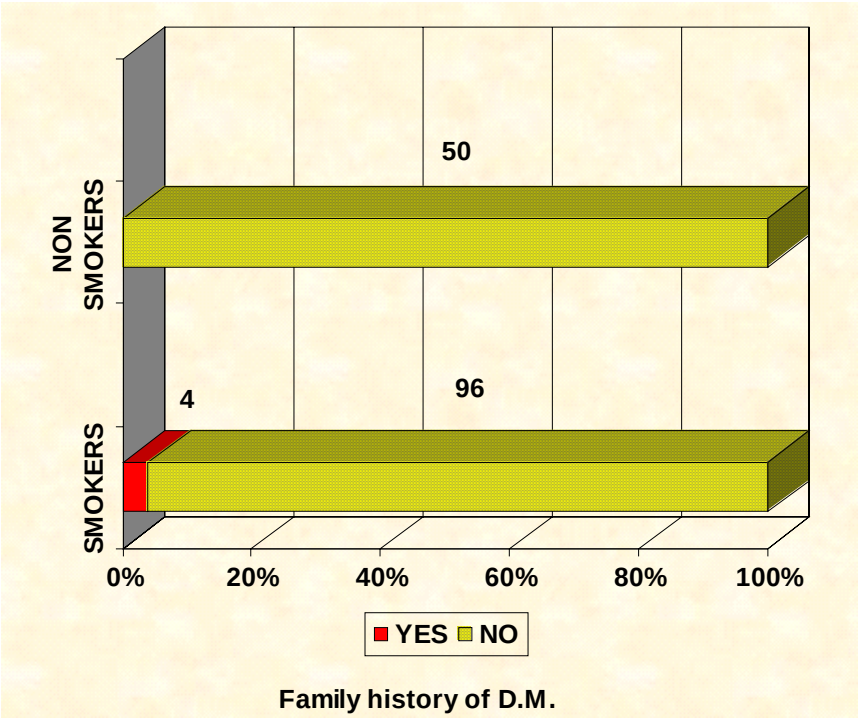


Table 5

Physical Activity

Life style (Physical Activity)	**Cases (Smokers)**		**Controls (Non Smokers)**	
	No	**%**	**No**	**%**
Sedentary	4	4	4	8
Non – sedentary	96	96	46	92
P	0.4415 (Not Significant)			

Majority of the population study in both cases and controls had non sedentary life style. Thus there was no significant difference between cases and controls with respect to lifestyle habits (‘p’ = 0.44)

Table 6

Smoking Profiles

Smoking Profile	Cases = 100 Controls = 50	
	No	**%**
A. Smoking (n = 150)		
a i) Current smokers	83	55.3
a ii) Former smokers	17	11.3
a) Total smokers	100	66.6
b) Non smokers	50	33.3
B. Type of Smoking (n = 100)		
a) Cigarettes	27	27
b) Bidis	47	47
c) Both	26	26
	Mean	**S.D**
C. Duration of smoking in years	20.54	9.75
D. No. per day	10.15	5.89
E. Pack years	10.4	8.6

Majority of the study population were current smokers (55.3%). Among the smokers, most of then were found to be Bidi smokers (47%).

SMOKING PROFILE

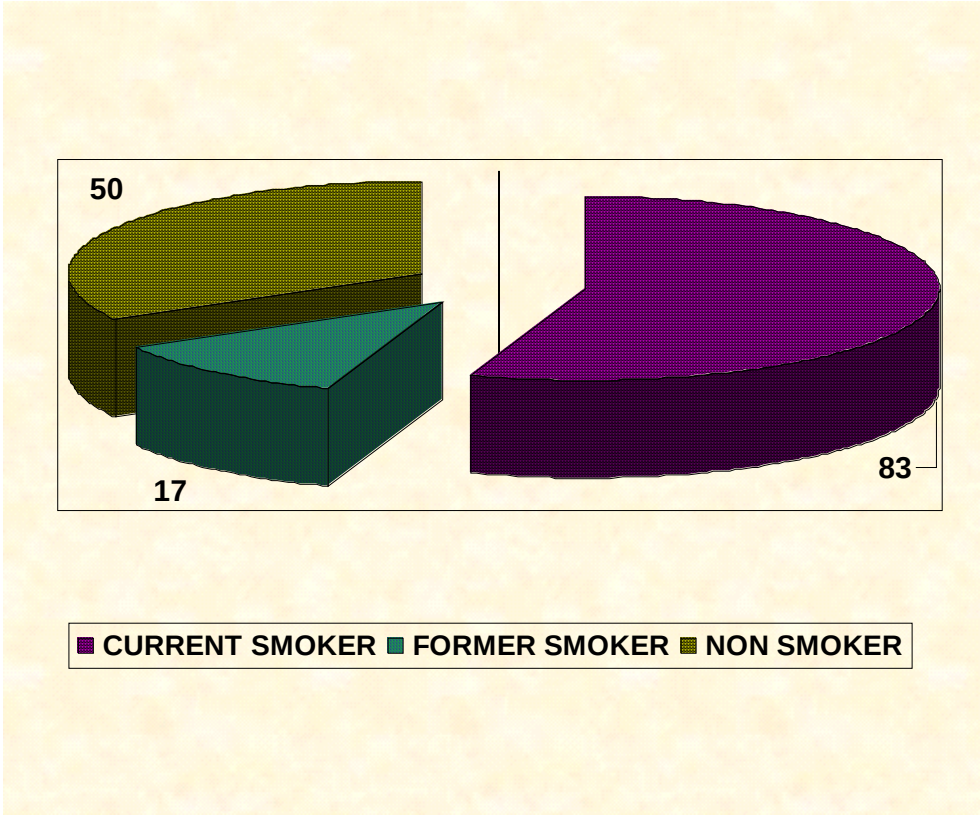


Table 7

Physical profile

Parameter	Cases (Smokers)		Controls (Non Smokers)	
	No	**%**	**No**	**%**
A. Body mass index(BMI)				
i) Normal (< 25)	70	70	45	90
ii) Over weight (25 – 29.9)	25	25	4	8
iii) obese (30 and above)	5	5	1	2
'P'	0.0116 Significant			
B. Blood pressure(BP)				
i) Normal	80	80	43	86
ii) Abnormal	20	20	7	14
'P'	0.4989 Not significant			
C. Waist Circumference				
i) Normal (m < 102 F $\leq$ 88)	97	97	50	100
ii) Abnormal (m > 102 F > 88)	3	3	-	-
'P'	0.5511 Not Significant			
D. Fasting Blood Sugar				
i) Normal (Less than 100mg/dl)	71	71	39	78
ii) Impaired (100 – 125)	12	12	11	22
iii) Diabetes (more than 125)	17	17	-	-
'P'	0.4727 Not significant			

Nearly 5% of the case population were obese. Among the control population, obesity accounted for 2% of them. There was a significant statistical difference between cases and controls with respect to BMI ('p' = 0.0116).

With regard to Blood Pressure, there was no significant statistical difference between cases and controls ('p' = 0.4989).

Glucose Intolerance among case population were found to be 29% and among the control population, found to be 22%. Thus there was no significant statistical difference between cases and controls ('p' = 0.4727).

BMI & SMOKING

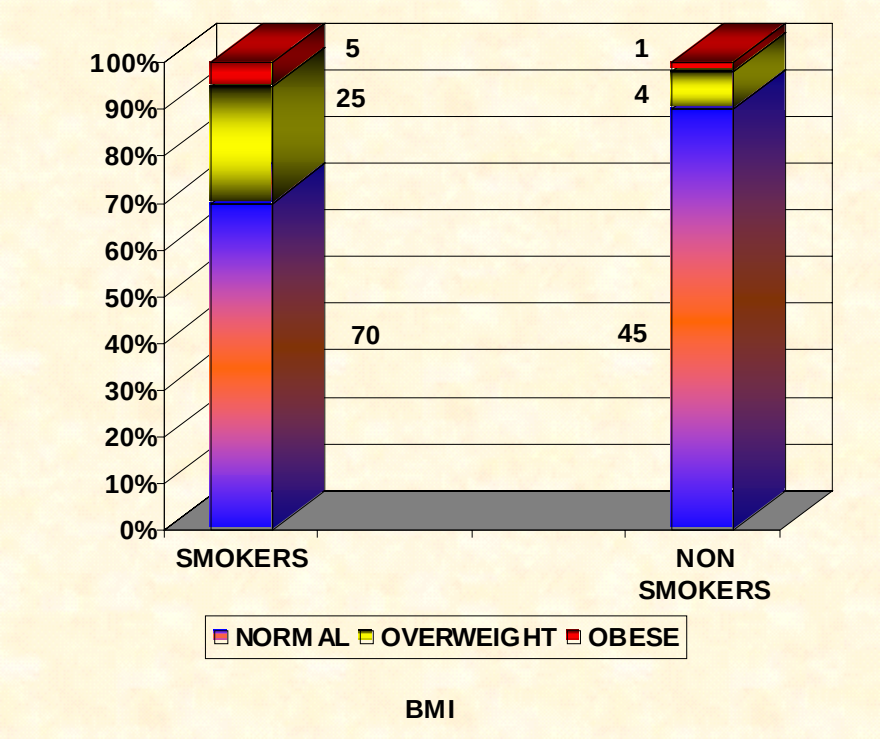

100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
5
25
70
1
4
45
SMOKERS
NON SMOKERS
NORMAL
OVERWEIGHT
OBESE
BMI

Table 8

Lipid Profile

Parameter	Cases (Smokers)		Controls (Non Smokers)	
	No	**%**	**No**	**%**
A. Triglyceride(TGL)				
i) Normal (≤ 150)	47	47	27	54
ii) Abnormal (> 150)	53	53	23	46
'P'	0.5253 (Not Significant)			
B. HDL				
i) Normal (≥ 40)	87	87	43	86
ii) Abnormal (< 40)	13	13	7	14
'P'	0.9323 (Not Significant)			

53 cases of the study group (53%) had high Triglyceride. 46% of the control group had high TG. Thus, there was no significant statistical association between study and control group (p =0.52)

13 cases of the study group (13%) had low HDL. 14% of the control group also had low HDL. Thus there was no significant statistical association between study and control group (p = 0.93)

Table 9

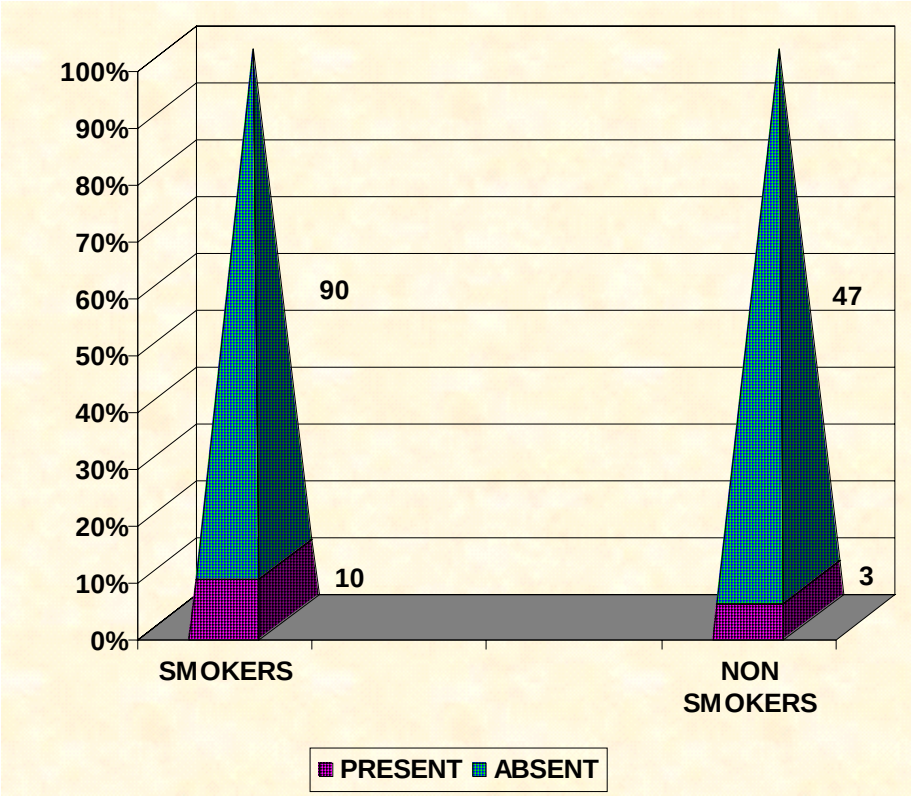
Metabolic Syndrome

Abnormalities	Smokers		Non Smokers	
	No	**%**	**No**	**%**
a) Central obesity (Waist circumference M > 102 cm F > 88 cm)	3	3	-	-
b) Abnormal TGL (> 150)	53	53	23	46
c) Abnormal HDL (< 40)	13	13	7	14
d) Hypertension (systolic B.P ≥ 130, Diastolic B.P ≥85)	20	20	7	14
e) Fasting blood glucose (≥100)	29	29	11	22
Metabolic syndrome(any 3 of the above)	10	10	3	6
'P'	0.3127 Not Significant			

TGL :Triglyceride , HDL:High Density Lipoprotein, B.P: Blood Pressure

10% of the case population had metabolic syndrome and 6% of the control population had the same. There was no significant statistical association

METABOLIC SYNDROME



B. RELATIONSHIP BETWEEN GLYCEMIC STATUS AND VARIOUS PARAMETERS.

Table 10

Age and Glycemic Status

Gly. Status	Age in years					
	Smokers		Non smokers		Total	
	Mean	SD	Mean	SD	Mean	SD
Normal	46.3	10.8	47.4	6.5	46.7	9.4
Impaired (prediabetes)	53.4	11.9	48.5	8.5	51.1	10.5
Diabetes	47.5	9.1	-	-	47.5	9.1
'P'	0.2714 Not Significant		0.3653 Not Significant		0.2009 Not Significant	

No statistically significant relationship existed between age and glycemic status.

Table 11

Glycemic status and smoking

Gly. Status	Smokers				Total Smokers		Non Smokers	
	Current		Former					
	Mean	%	Mean	%	Mean	%	Mean	%
Normal (110)	60	54.5	11	10	71	64.5	39	35.5
Impaired (23)	9	39.1	3	13	12	52.5	11	47.8
Diabetes (17)	14	82.4	3	7.6	17	100	-	-
'p' smokers vs non smokers	**0.0048 Significant**							
Current smokers vs non smokers	0.0055 (Significant)							
Former smokers vs non smokers	0.0142 (Significant)							
Current smokers vs Former smokers	0.5884 (Not significant)							

There was a significant statistical association between smoking and glycemic status (p = 0.0048). There was no statistically significant difference between current smokers and former smokers.

GLYCEMIC STATUS & SMOKING

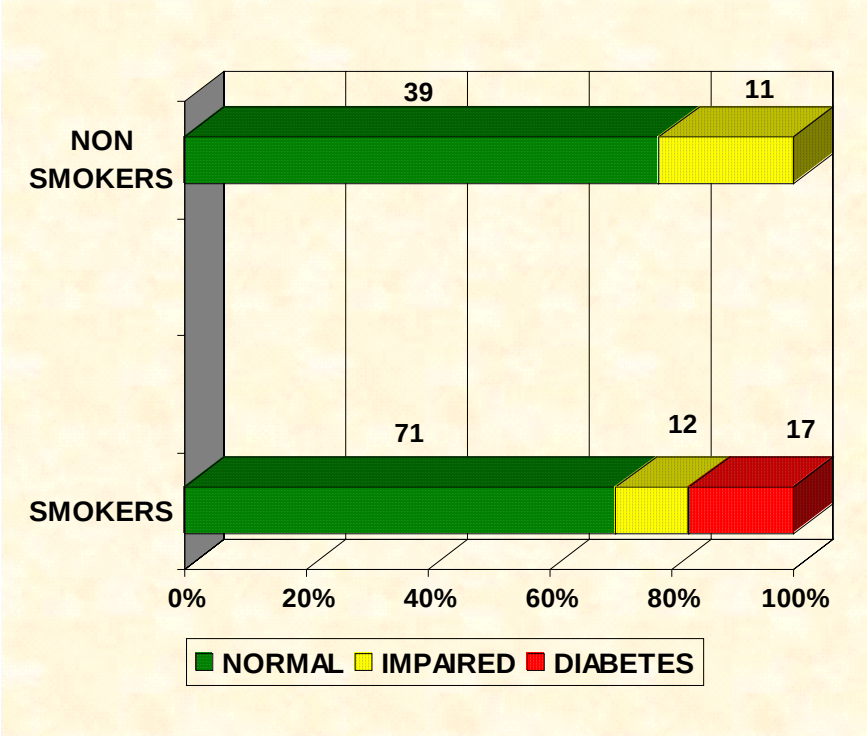


Table 12

Type of Smoking and Glycemic status

Smoking type	Glycemic status					
	Normal		Impaired		Diabetes	
	No	%	No	%	No	%
Cigarettes (27)	20	74.1	3	11.1	4	14.8
Bidis (47)	34	72.3	6	12.8	7	14.9
Both (26)	17	65.4	3	11.5	6	23.1

There is no significant difference between glycemic status of smokers and type of smoking.

TYPE OF SMOKING & GLYCEMIC STATUS

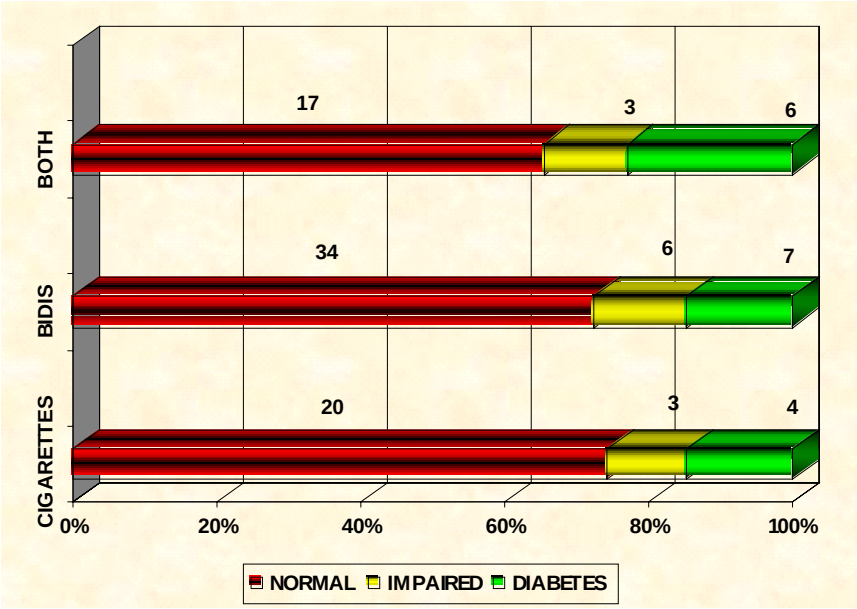


Table 13

Metabolic syndrome and smoking

Metabolic syndrome	Smokers						Non Smokers	
	Current		Former		Total			
	No	%	No	%	No	%	No	%
Present (13)	7	53.8	3	23.1	10	76.9	3	23.1
Absent (137)	76	55.5	14	10.2	90	65.7	47	34.3
'p' value for Current vs nonsmokers	0.4403 not significant							
'p' value for Former vs nonsmokers	0.167 not significant							
'p' value for total smokers and non-smokers	0.5452 Not significant							

No statistically significant relationship exist between smoking and metabolic syndrome.

METABOLIC SYNDROME & SMOKING

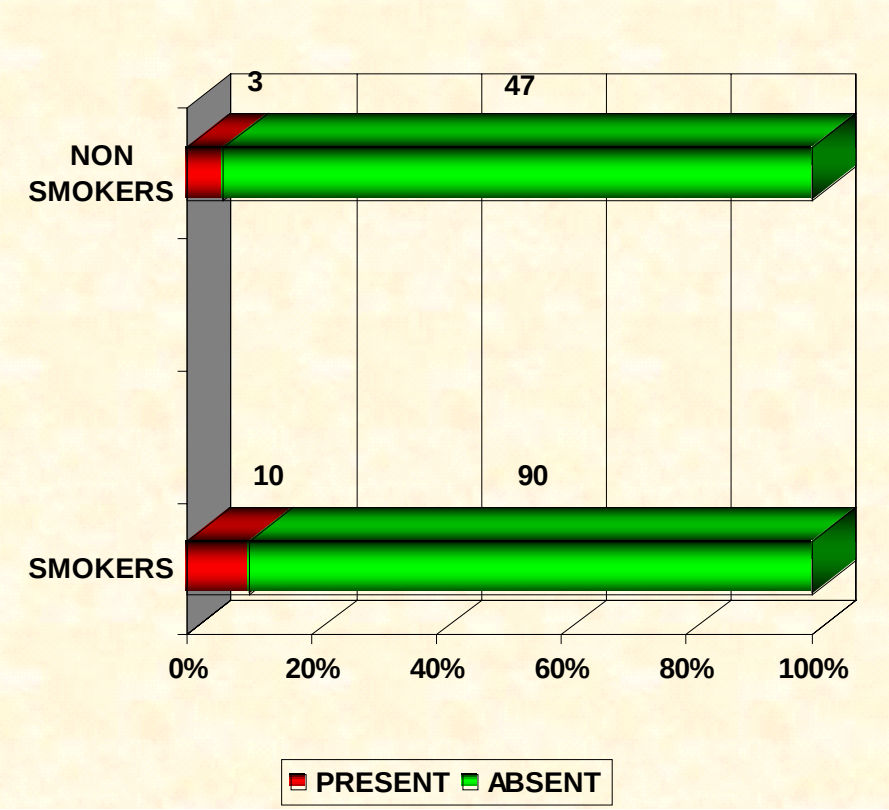


Table 14

Pack years and Glycemic Status

Glycemic Status	**Pack years for**					
	Current smokers		**Former smokers**		**Total**	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Normal	9.4	8.5	8.9	8.3	9.3	8.4
Impaired	11.8	7.4	13.4	14.5	12.2	8.9
Diabetes	12.7	9.1	18.0	6.1	13.6	8.1
'p'	0.1525 Not Significant		0.224 Not Significant		**0.0483 Significant**	

Statistically significant. relationship exists between pack years of total smokers and glycemic status (p. 0.0483)

GLYCEMIC STATUS & PACK YEARS

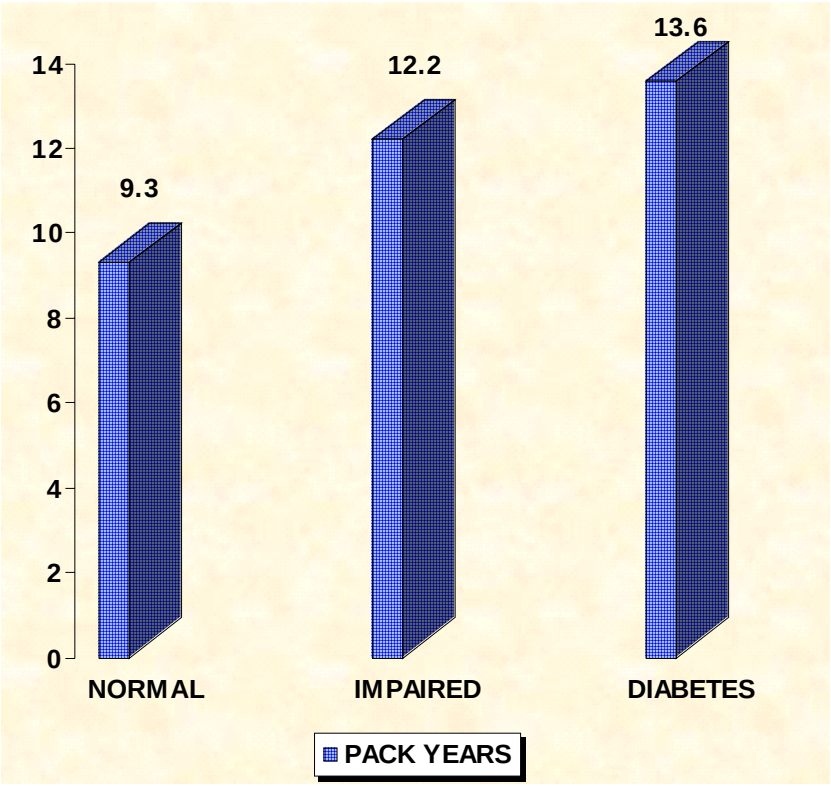


Table 15

Pack years and metabolic syndrome

Metabolic syndrome	Pack years for					
	Current smokers		Former smokers		Total	
	Mean	SD	Mean	SD	Mean	SD
Present	17.5	17.9	8.4	6.2	14.8	15.5
Absent	9.5	6.9	11.9	9.9	9.9	7.4
'p'	0.2578 Not Significant		0.7526 Not Significant		0.4343 Not Significant	

No statistical significant association exist between pack years and metabolic syndrome.

PACK YEARS & METABOLIC SYNDROME

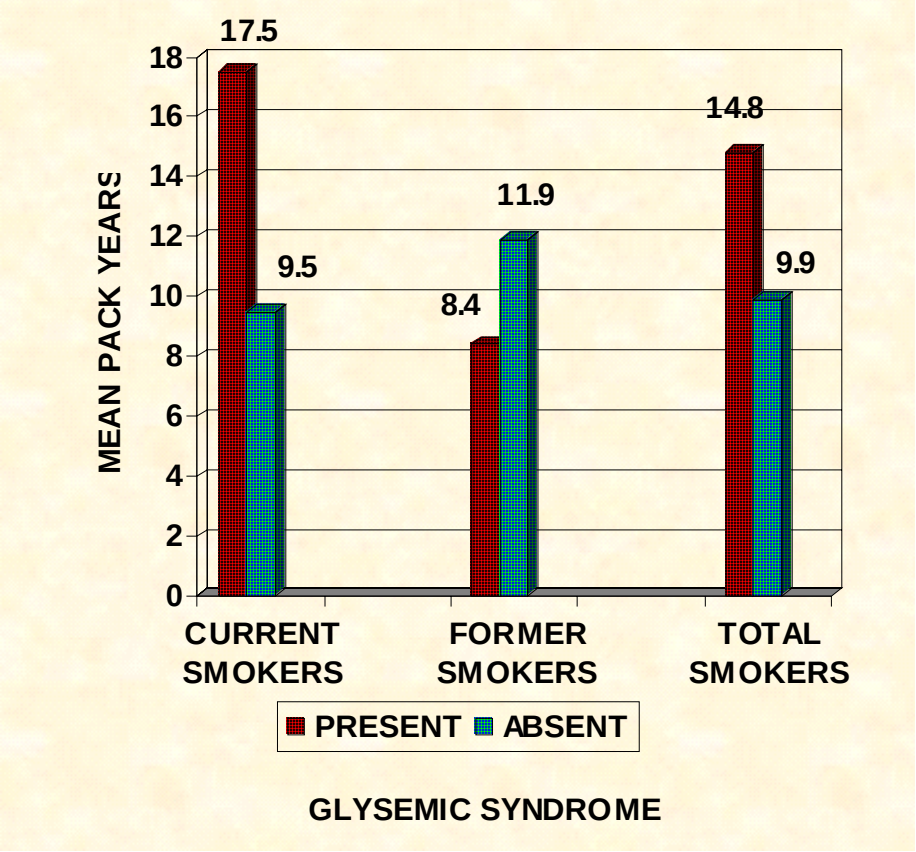


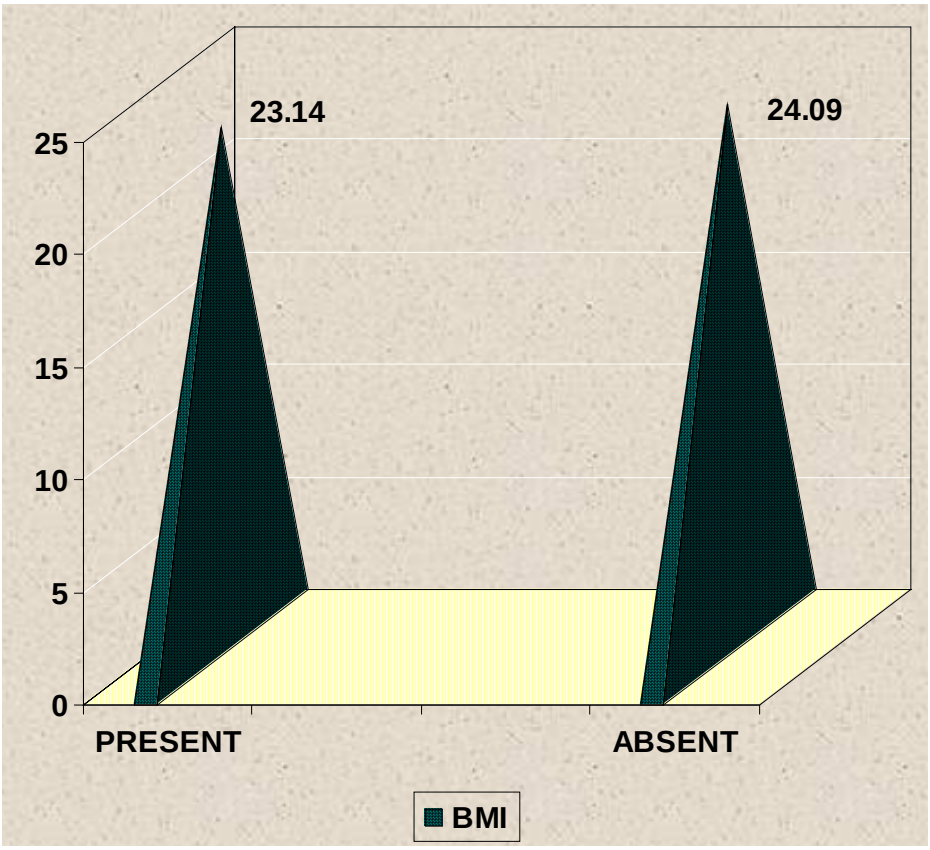
Table 16

Body Mass Index and Metabolic syndrome

Metabolic syndrome	BMI	
	Mean	**S.D.**
Present	23.14	3.33
Absent	24.09	3.85
'p'	0.4706 Not Significant	

No statistically significant. relationship exists between BMI and metabolic syndrome (p.= 0.4706)

METABOLIC SYNDROME & BMI



DISCUSSION

DISCUSSION

Among the 150 participants in my study, 100 of them were smokers. Among the 100 smokers, 83 were current smokers and 17 were former smokers.

The mean age of the participants was 47 (SD 10.7) years, majority of the smokers had an occupation of daily wages labourers and a low educational status

Smoking and Educational status

In my study, Tobacco consumption in the form of smoking was observed more among low educational status (Up to 5^{th} standard – 45%) and illiterates (21%), compared to those educated higher (>5^{th} std – 34%) In (Rajeev Gupta et al 2006)[47] study, the greatest tobacco consumption was observed among illiterate (60%) and low education status (51%), compared to more literate (6^{th} -10^{th} and > 10 years of formal education-46 and 36% respectively)

Thus, by comparing both thus status, we observe **an inverse association of education status with tobacco use.** In my study, low

educational status were found to smoke more compared to illiterate on the contrary of Rajeev et al study.[47]

This difference in the above could be explained as follows: My study included 100 cases , compared to their study (3148 cases). My study included tobacco consumption only in the form of smoking in contrast to their study which included other forms of tobacco use in addition to smoking.

Glucose Intolerance and smoking

In my study, 12 participants out of 100 smokers had impaired fasting glucose and 17 cases had diabetes. The prevalence of glucose intolerance was also higher among smokers than is non smokers (p. =0.004).

A prospective study by Houston et al,[31] showed a graded association between smoking exposure and the development of glucose Intolerance. The 15 year incidence of glucose intolerance was highest among smokers (21.8%) followed by never smokes with passive smoking exposure (17.2%), and then previous smokers (14.4%); It was lowest for never smokers with no passive exposure (11.5%). Thus, their study ended up by stating that current smokers and never smokers with passive smoking exposure were at higher risk than never smokers without passive smokers exposure and risk in previous smokers was similar to that is never smokers without passive smoking

exposure. In my study, which was a cross sectional study, there was a significant statistical association between smoking and glycemic status (p' 0.0048). My study also showed that a statistically significant association between current smokers and non smokers (p' 0.0055) similar to the study by Houston et al [31].But, in contrary to the study by Houston et al [31], which said that risk is previous smokers was similar to that of never smokers without passive smoking exposure, my study showed a significant statistical association between former smokers and non smokers ('p' 0.0142). This may be due to the fact that, my study did not subcategorized never smokers as, those with passive exposure and without passive exposure. But, there are certain studies which supported the fact that former smokers were also at risk for Diabetes.

Carolie et al[9] conducted a systematic review and meta-analysis of studies describing the association between active smoking and incidence of diabetes or other glucose intolerance which also indicated that active smokers had 44% increased risk for developing type 2 diabetes compared with Non smokers. They also described a significant association between former smokers and incidence of diabetes.

In another study by Sulander T. et al[59], they found that heavy smokers and current smokers were at risk of obesity and diabetes.

A study Beziaud et al (2004)[8] also concluded that current and past smoking were associated with a risk of diabetes mellitus essentially in men. Thus the statistical association between former smokers & glycemic status was supported by the above studies.

Thus, my study clears correlates with many trials, which showed an increased risk of developing diabetes among smokers (current and former).

Type of smoking and glycemic status

In the present study, smokers showed an increased risk for glucose intolerance, but the type of smoking did not influence the result.

Pack years and glycemic status

In my study, the pack years among participants with normal glycemic status had a mean of 9.3 (S.D 8.4) ; participants with impaired fasting glucose had a mean of 12.2 (S.D 8.9) and those with diabetes had a mean of 13.6 (S.D 8.7). Thus, increase in pack years of smoking among the participate was associated with an increased risk of developing glucose intolerance.

In Houston, et al study[31], increase in pack years of smoking over time among the 4572 participants was associated with an increased risk of developing glucose intolerance.

Carolie et al study[9] also concluded that there was a dose-response relationship, with stronger associations for heavy smokers relative to lighter smokers and for active smokers relative to former smokers.

Thus, use of Pack Years of smoking showed a consistent dose– response effect of increasing risk with increasing exposure to tobacco.

However, In the present study, the dose-response relationship did not correlate foractive smokers relative to former smokers. Beziaud et al study[8] found that the association to diabetes was similar in current and former smokers, and no dose-effect relationship was found.

Capri Gabrielle Foy et al study[11] found that participants with impaired glucose tolerance were not associated with significantly higher incidence of diabetes compared with never smokers.

Smoking and BMI

We found that among participants, smoking had a significantly higher incidence of obesity compared to never smokers.

In a study by Sulander T et al study [59](2007) , they found that, "compared to non-smokers, ex-heavy smokers had higher and current light smokers lower relative risk of obesity".

In another study by Arnaud Chiolero et al[13] (2007), obesity was associated in a graded manner with the number of cigarettes daily smoked, particularly in men.

Rasky E et al[46] (1996) study found that heavy smoking as well as smoking cessation were significantly correlated with higher relative weight.

Endocrine abstracts[20] (2006) also concludes in its study by stating that there was a U –shaped association between smoking and BMI. They also concluded that heavy smokers were associated with an unhealthy lifestyle, which appeared to override weight reducing effect of cigarette smoking.

Thus, the present study correlates that smoking is positively related to body weight. Most of the participants in our study also found to smoke a lot, which also favours our study of increased BMI

Smoking and metabolic syndrome

Of the components of the metabolic syndrome, we could find a significant association for fasting plasma glucose. but we could not find a significant association with other factors.

In my study, thus smoking did not show statistically significant correlation to metabolic syndrome compared to non smokers. This study is somewhat contrary to the general concept that cigarette smoking is independently associated with metabolic syndrome.

We suppose that the cross sectional design of this study limited its ability to detect these associations.

SUMMARY

SUMMARY

The study "IMPACT OF SMOKING ON GLYCEMIC STATUS" was conducted among 150 patients attending government Rajaji Hospital, Madurai.

From the patients who satisfied inclusion criteria, study was conducted and the relationship between smoking and glucose intolerance was evaluated

.

Significant statistical association was noted with respect to the following

- Smoking and glucose intolerance
- Pack years of smoking and glucose intolerance
- Smoking and BMI

No statistically significant relationship was noted for the following

- Type of smoking and glucose intolerance
- Smoking and metabolic syndrome

CONCLUSION

- Tobacco smoking showed a significant positive association with glucose intolerance/diabetes, the possible operative mechanisms being

1. Smoking stimulate symathetic system, which in turn leads to an elevated catecholamine levels and there by insulin resistence.
2. Smoking influences visceral adipose tissue and there by insulin resistance.
3. Smokers(especially heavy smokers) are prone for unhealthy food habits and low physical activity which in turn leads to visceral fat accumulation and insulin resistance.
4. Smoking directly influences insulin sensitivity and impaires insulin action.

- The pack years of exposure showed a significant positive association with glucose intolerance/diabetes. The mean packyears among patients with glucose intolerance is 11.8 and the mean pack years among patients with frank diabetes is 12.7.Thus, the risk of diabetes directly correlates with the packyears in my study. As the packyears increases, the risk of diabetes also increases.

- There is a significant positive association between tobacco smoking and increased BMI; this is explainable as follows: smokers are prone for unhealthy diet and low physical activity, thus leading on to visceral fat accumulation and insulin resistance.

- There is no significant difference among types of smoking (bidis, cigarettes, both) and glucose intolerance.

What is already known on this topic

- Smoking is hypothesised to increase insulin resistance.

- Results of previous observational studies assessing the association of smoking and incidence of diabetes have been mixed

What this study adds

- A strong positive association existed between tobacco smoking and glucose intolerance / frank diabetes
- Among smokers, total pack years smoked was associated with increased risk of glucose intolerance/diabetes

LIMITATIONS

- Some parameters such as serum cotinine concentration (a biochemical marker of nicotine uptake) which defines the tobacco exposure level was not taken in my study due to non availability of laboratory support.

- Also the present study represents people recruited from those attending government Rajaji Hospital in Madurai. Our results are not necessarily generalized to other ethnic population.

- My study could not demonstrate the association between smoking and metabolic syndrome.

- The cross sectional design of this study prohibited me from concluding causal relationship and may have included some bias. We need further evidence on the consistency of the association in different populations ideally from cohort studies with fasting glucose measurements at baseline and follow-up. We also need a well-designed clinical studies of the effects of acute and chronic smoking on insulin resistance.

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ABBREVATIONS

PVD	-	Peripheral vascular disease
CAD	-	Coronary artery disease
PROM	-	Premature rupture of membrane
IRDS	-	Infant respiratory distress syndrome
ARMD	-	Age related macular degeneration
HC	-	Hip circumference
WC	-	Waist circumference
WHR	-	Waist hip ratio
VAT	-	Visceral adipose tissue
BMI	-	Body mass index
OCP	-	Oral contraceptive pill
TC	-	Total cholesterol
TGL	-	Triglyceride

HDL	-	High density lipoprotein
VLDL	-	Very low density lipoprotein
LDL	-	Low density lipoprotein
Ht	-	Height
Wt	-	Weight
BP	-	Blood pressure
Blood sugar(F)	-	Fasting
Blood sugar(pp)	-	Postprandial
NCEP: ATPIII	-	National Cholesterol Education Programme, Adult Treatment Panel III

PROFOMA – IMPACT OF SMOKING ON GLYCEMIC STATUS

NAME	
AGE	
SEX	
OCCUPATION	
EDUCATIONAL STATUS	
FAMILY H/O DIABETES	
DIET & PHYSICAL ACTIVITY	
COMORBID ILLNESS	
SMOKING 1) NEVER/FURMER/ CURRENT 2) TYPE OF SMOKING (CIGARS / BIDIS / BOTH) 3) NO OF CIGARS ; < 0R > 20 PER WEEK	
ALCOHOLISM	
EXAMINATION 1) weight 2) height 3) blood pressure 4) waist hip ratio	
INVESTIGATIONS BLOOD SUGAR fasting – Post prandial SERUM LIPID PROFILE (fasting)	